Amendments to the Drawings

Please insert Figures 6 and 7 after Figure 5.

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1 and 10-74 are pending in the application, with claims 1, 49, and 66 being the independent claims. Claims 2-9 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 10-74 are sought to be added. The specification is also sought to be amended. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Support for the amended claim 1 and new claims 10-74 can be found in the specification and claims as originally filed. Further, support for the new claims 10-74 can be found in the parent Appl. No. 10/629,308 ('the '308 application), filed July 29, 2003, that is incorporated by reference in its entirety.

Specifically, support for the amendment to claim 1 can be found, *inter alia*, in original claim 5. Support for new claims 10-15 can be found, *inter alia*, in original claim 3. Support for new claim 16 can be found in original claim 2, subpart a. Support for new claim 17 can be found at page 15, line 15, of the specification as originally filed. Support for new claim 18 can be found in original claim 2, subpart b. Support for claim 19 can be found at page 5, line 21, of the specification as originally filed. Support for claim 20 can be found in original claim 2, subpart d and at page 15, line 22, of the specification as originally filed.

Support for claim 21 is found at page 15, lines 2-3, of the specification as originally filed. Support for claim 22 can be found at page 14, line 31, of the

specification as originally filed. Support for claim 23 is found in original claim 4, subpart a. Support for claim 24 can be found at page 15, lines 4-5, of the specification as originally filed. Support for claim 25 can be found at page 15, line 5, of the original specification. Support for claim 26 can be found in original claim 4, subpart b and at page 5, lines 27-28, of the original specification. Support for claim 27 can be found in original claim 4, subpart c and at page 5, line 15, of the original specification. Support for new claim 28 is found in original claim 4, subpart d.

Support for new claims 29 and 30 is found in original claim 5, subparts d and e, respectively. Support for claim 31 can be found at page 34, Table I, of the original specification.

Support for claim 32 can be found at page 17, lines 18-19 of the original specification. Support for claim 33 can be found in original claim 6, subpart b and at page 18, lines 5-6, of the original specification. Support for claim 34 can be found at page 18, line 6 of the original specification.

Support for new claims 35-37 is found in original claim 6, subparts c, d, and f, respectively.

Support for new claim 38 can be found at page 5, lines 9-16. Support for new claim 39 is found in original claim 7, subpart a. Support for claims 40-41 is found in original claim 7, subparts c-d, respectively. Support for new claim 42 is found in original claim 7, subpart g. Support for claim 43 is found in original claim 7, subpart i. Support for claims 44-46 can be found in claim 7, subparts k-m, respectively. Support for claim 47 can be found at page 21, lines 19-21, of the parent '308 application as filed.

Support for claim 48 can be found in claim 6, subpart i of the originally filed parent '308 application.

Support for claim 49 can be found, *inter alia*, in original claim 1, at page 5, lines 23-24, and at page 6, line 17, of the originally filed specification. Support for claim 50 can be found, *inter alia*, in original claim 1, at page 20, lines 12-13 of the original '308 application, and at page 6, line 17, of the present specification as filed. Support for claims 51 and 52 is found in the original claim 7, subparts e and f, respectively. Support for claims 53 and 54 is found in original claim 7, subparts h and j, respectively. Support for claim 55 can be found at page 8, lines 4-6, of the specification as originally filed. Claims 56 and 57 are supported by claim 6, subparts g and j, respectively, of the parent '308 application.

Claim 58 is supported at page 17, lines 18-19, of the original specification. Support for claim 59 can be found in the original claim 8, subpart a and at page 18, lines 5-6, of the original specification.

Claims 60 and 61 are supported by original claim 6, subparts c and e, respectively.

Support for claim 62 can be found at page 24, lines 13-15, of the original parent '308 application. Support for claim 63 is found in claim 14, subpart y of the parent '308 application.

Support for claim 64 is found at page 14, lines 1-3, of the specification as originally filed. Support for claim 65 can be found, *inter alia*, at page 5, line 13, of the original specification.

Support for claim 69 can be found, *inter alia*, in original claims 1 and 6, at page 5, line 24 and at page 12, line 23, of the originally filed specification. Support for claims 67 and 68 can be found in original claim 6. Support for claim 69 is found in original claim 7, subpart n. Support for claim 70 is found in original claim 7, subpart b.

Support for new claim 71 can be found in original claims 1 and 5, at page 19, lines 1-5, and at page 21, line 28, of the specification as originally filed.

Support for new claim 72 can be found, *inter alia*, in original claim 1, at page 5, lines 23-24, at page 6, line 17, and at page 22, line 15, of the originally filed specification.

Support for claim 73 can be found, *inter alia*, in original claim 9. Support for claim 74 can be found at page 28, lines 5-9, of the specification as originally filed.

The specification has been amended by adding paragraphs from the parent '308 application directed to the present invention. Support for the text to be added at page 12 of the specification after the first full paragraph has support in the parent '308 application as follows: at page 20, line 4 through page 24, line 12; at page 25, line 26 through page 26, line 10; at page 27, lines 1-28; and at page 28, lines 21-24.

Support for the text to be added at page 38, above the title "8. REFERENCES CITED" has support in the parent '308 application as follows: Examples 1, 2, 3, 4, 5, 6, 7, and 8 are Examples 3, 4, 6, 7, 8, 9, 12, and 13, respectively.

Figures 6 and 7 have also been inserted into the specification after Figure 5. Figures 6 and 7 are supported by Figures 1 and 2 of the parent '308 application. As such, no new matter has been added.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Objection to the Specification

The Examiner has objected to the specification because of the use of trademarks. The Examiner states that trademarks should be capitalized where they appear and that they should be accompanied by the generic terminology. The Examiner further requires that the ingredients contained in the PROPOFLO™ and RAPINOVET™ at the time of the invention should be listed. Applicants respectfully traverse this objection.

It is respectfully submitted that the trademarks used in the application have already been properly identified by a proper trademark symbol ® or ™. Therefore, it is not necessary to capitalize the trademarks. Further, the ingredients contained in PROPOFLO™ and RAPINOVET™ at the time of the invention have already been listed in the original specification at page 2, lines 26-28 and at page 3, lines 3-6, of the originally filed specification, respectively.

Reconsideration and withdrawal of the objection to the specification is respectfully requested.

Rejections under 35 U.S.C. § 102

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir.

1987). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic v. Genentech, Inc.*, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991).

The Examiner has rejected claims 1 and 2 under 35 U.S.C. § 102(b) as allegedly being unpatentable by Glen *et al.* (U.S. 4,056,635). Applicants respectfully traverse this rejection.

The Examiner states that Glen *et al.* disclose an aqueous composition containing a block copolymer (column 3, line 27), a polyethylene glycol (column 3, lines 29-30), and 2,6-diisopropylphenol (column 3, lines 23-24) as claimed in claim 1. Applicants have amended claim 1 by requiring that propylene glycol is present in the aqueous composition in addition to a block copolymer, a polyethylene glycol, and 2,6-diisopropylphenol. It is respectfully submitted that Glen *et al.* do not anticipate the formulation as claimed in amended claim 1 at least because the reference does not describe each and every element of claim 1.

Further, is respectfully submitted that Glen *et al.* do not anticipate claim 49, claim 66, claim 71, or claim 72.

In view of the above, it is respectfully submitted that Glen *et al.* do not anticipate any of the claims 1 and 10-74. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1 and 2 are respectfully requested. Claim 2 has been canceled.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 1-6 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Glen *et al.* (U.S. 4,056,635), May *et al.* (U.S. 6,140,374), and Lee *et al.* (U.S. 6,743,436 B1). Applicants respectfully traverse this rejection.

In determining the differences between the prior art and the claims, the question under 35 U.S.C. § 103 is not whether the differences *themselves* would have been obvious, but whether the claimed invention *as a whole* would have been obvious. *See* M.P.E.P. § 2141.02. Thus, *all* the limitations of a claim must be considered when weighing the differences between the claimed invention and the prior art in determining the obviousness of a process or a method claim. *See* M.P.E.P. § 2116.01. Furthermore, a prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 861 (1984).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *See* M.P.E.P. § 2143.

The Examiner states as follows:

> Glen teaches an aqueous composition containing (claim 1 and 3), a block copolymer (column 3 line 27 to be P188 which is the same as Pluronic F68), a polyethylene glycol (column) 3 lines 29-30), to be (PEG-200, 400, 600 as in claim 4) and 2,6-diisopropylphenol (column 3 line 23-24 as in claim 1). Glen also teach a formulation (claim 2) according to claim 1, where in the amount of 2,6-diisopropylphenol is at least 15 (w/v) of said formulation (column 3 line 22 see also line 62), from 1 to 5% (w/v) of said formulation (column 3 line 22 see also line 62), from 1 to 2% (w/v) of said formulation (column 3 line 22), 1% (w/v) of said formulation (column 3 line 65), a tonicity modifier to be dextrose (claim 5) at column 3 line 31, propylene glycol (column 3 line 29 as in claim 5), a formulation which further comprises citric acid (column 3 line 10 as in claim 6,). Glen also teach administering formulation as in claim 1 to a patient as an anesthetic, by administering an anesthetically effective amount of propofol.

The Examiner further states that May *et al.* teach a sterile pharmaceutical composition/formulation having different amount of 2,6-diisopropylphenol, and the incorporation of benzyl alcohol and disodium EDTA.

The Examiner alleges that Lee *et al.* teach an aqueous solution comprising a poloxamer 188 in an amount of 8%, 4 % PEG-400 and 1% propofol in Example 7 (at column 7).

The Examiner follows that

> [t]he claims differ where Glen did not per se teach the combination in concentration of the block polymer to be 6 and 8% as claimed by applicant, nor of the polyethylene glycol concentration to be 2% not the concentration of citric acid as in claim 8. However the patent teach a wide concentration range for co-polymer as 10-20%, polyethylene glycol

5-20%, citric acid as 0.1% used to maintain the pH value of the formulation instead of an antimicrobial agent.

The Examiner alleges that it would have been obvious to one skilled in the art at the time the claimed invention was made to formulate a sterile composition replacing the concentration ranges disclosed by Glen *et al.* with those claimed. The Examiner states that although Glen *et al.* did not per se teach the exact concentrations of the components, Lee *et al.* provided motivation to optimize the ranges of surfactants. Furthermore, the Examiner alleges that one of ordinary skill in the art would have been motivated to combine the teachings of Glen *et al.* with that of May *et al.* and Lee *et al.* resulting in the concentrations as claimed and obtain successful results in administering the formulation as an anesthetic to patients.

Applicants respectfully disagree. It is respectfully submitted that the Examiner has failed to establish a *prima facie* case of obviousness. In particular, neither Glen *et al.*, May *et al.* or Lee *et al.* teach or suggest, alone or in combination, all the claim limitations. Further, Glen *et al.*, May *et al.* or Lee *et al.*, alone or in combination, do not provide any motivation for a person skilled in the art to prepare an aqueous formulation comprising 1,2-diisopropylphenol as recited in amended claim 1 or in new claims 49, 66, 71, and 72. Furthermore, Glen *et al.*, May *et al.* and Lee *et al.* teach away from the present invention.

Glen *et al.* purportedly describe a sterile aqueous composition containing "from 1 to 5% by weight, especially from 1 to 2% by weight and particularly 2% by weight of 2,6-diisopropylphenol; 10 to 20% by weight of . . . a polyoxyethylene-polyoxypropylene block copolymer, especially 'Pluronic' F68; and **optionally** from 5 to 20% by weight of

ethanol, propylene glycol **or** polyethylene glycol . . ." (See col. 3, lines 21-30, emphasis added). Thus, one of the components ethanol, propylene glycol or polyethylene glycol is optional in the aqueous composition containing 2,6-diisopropylphenol and a block copolymer. Glen *et al.* do not describe any aqueous composition containing, in addition to 2,6-diisopropylphenol and a block copolymer, both a polyethylene glycol and propylene glycol as claimed in claim 1 as amended and, therefore, Glen *et al.* do not teach or suggest all the limitations.

May *et al.* purportedly describe an oil-in-water emulsion containing 2,6-diisopropylphenol and a surfactant, for example ethoxylated ethers and ethoxylated esters, polypropylene polyethylene block copolymers, and phosphatides, and preferably the surfactant is egg phosphatide (see col. 2, lines 5-12). May *et al.* do not describe either a polyethylene glycol or a propylene glycol in the aqueous composition. Therefore, May *et al.* do not teach or suggest all the claim limitations of claim 1. Further, it is submitted that May *et al.* teach away from the formulations of the present invention by preferring the use of an egg phosphatide as a surfactant rather than a polypropylene polyethylene block copolymer. Thus, May *et al.* do not remedy the deficiencies of Glen *et al.*

Lee *et al.* purportedly describe an aqueous composition containing 2,6-diisopropylphenol and a poloxamer as a surfactant (col. 3, lines 10-11). This composition "may additionally contain at least one co-surfactant selected from the group consisting of SOLUTOL HS 15 (Macrogol-15 Hydroxystearate), egg lecithin, LABRASOL (Polyoxy capryllic glyceride), polyoxy 10 oleyl ether, TWEEN (polyoxyethylene sorbitan fatty acid esters), ethanol and polyethylene glycol . . ." (See

col. 3, lines 16-24). Lee *et al.* do not describe any composition containing polyethylene glycol and propylene glycol in addition to 2,6-diisopropylphenol and poloxamer as claimed in claim 1 and, therefore, the reference does not teach or suggest all the claim limitations.

Further, contrary to the Examiner, Lee *et al.* do not describe in Example 7 a composition containing 8% by weight poloxamer 188, 1% of propofol and 4% of PEG-400, but a composition containing 5% (w/v) of PEG-400.

It is respectfully submitted that Glen *et al.*, May *et al.* or Lee *et al.* do not provide any suggestion or motivation for a person skilled in the art to modify the formulations purportedly described in these references in order to arrive at the formulation as claimed in claim 1 with a reasonable expectation of success.

In view of the above, it is respectfully submitted that Glen *et al.*, May *et al.* or Lee *et al.*, alone or in combination, do not render claim 1, or any claim dependent from this claim, obvious. It is also submitted that Glen *et al.*, May *et al.* or Lee *et al.*, alone or in combination, do not render claim 49, 66, 71, or 72, or any claim dependent from these claims, obvious.

Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) of claims 1-6 are respectfully requested. Claims 2-6 have been canceled.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be

withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

John M. Covert
Attorney for Applicants
Registration No. 38,759

Date: Nov. 8, 2005

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

455457_3.DOC